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AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1-46. (Canceled)

47. (Currently amended) A composition comprising an effective amount of a compound of formula I:

]

or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle, wherein:

 R^{1} is $-(L)_{m}R$, $-(L)_{m}Ar^{1}$, or $-(L)_{m}Cy^{1}$;

L is -S-, -O-, -N(R)-, or a C_{1-6} alkylidene chain wherein up to two non-adjacent methylene units of L are optionally and independently replaced by -S-, -O-, -N(R)-, -N(R)C(O)-,

 $-N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO_2-, -C(O)-, -CO_2-,$

 $-C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO_2-, -SO_2N(R)-, -N(R)SO_2-, \\$

 $-N(R)SO_2N(R)$ -, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or $-C(O)CH_2C(O)$ -;

m is 0 or 1;

Ar¹ is an optionally substituted 5-7 membered monocyclic ring or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Cy¹ is an optionally substituted 3-7 membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen,

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oxygen, or sulfur, or an 8-10 membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein;

Ar¹ and Cy¹ are each optionally substituted with up to 5 occurrences of Z-R^X; wherein

each occurrence of Z is independently a bond or a $C_{1\mbox{-}6}$ alkylidene chain, wherein up to

two non-adjacent methylene units of Z are optionally replaced by -S-, -O-, -N(R)-,

 $-N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO_2-, -C(O)-,$

 $-CO_2-$, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, $-SO_2-$, $-SO_2N(R)-$, $-N(R)SO_2-$,

 $-N(R)SO_2N(R)$ -, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or $-C(O)CH_2C(O)$ -;

each occurrence of R^X is independently selected from -R', halogen, NO₂, CN, -OR', -SR',

 $-N(R')_2$, -N(R')C(O)R', -N(R')C(S)R', $-N(R')C(O)N(R')_2$, $-N(R')C(S)N(R')_2$,

 $-N(R')CO_2R'$, -C(O)R', -C(S)R', $-CO_2R'$, -OC(O)R', $-C(O)N(R')_2$, $-C(S)N(R')_2$,

 $-OC(O)N(R')_2$, -S(O)R', $-SO_2R'$, $-S(O)_3R'$; $-SO_2N(R')_2$, $-N(R')SO_2R'$,

 $-N(R')SO_2N(R')_2$, -C(O)C(O)R', $-C(O)CH_2C(O)R'$, -NR'NR'C(O)R',

-NR'NR'C(O)N(R')₂, -NR'NR'CO₂R', -C(O)N(OR') R', -C(NOR') R', -S(O)₃R,

-N(OR')R', $-C(=NH)-N(R')_2$; or $-(CH_2)_{0-2}NHC(O)R'$; wherein

each occurrence of R is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group,

- each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, an optionally substituted C_{6-10} aryl ring, an optionally substituted heteroaryl ring having 5-10 ring atoms, or an optionally substituted heterocyclyl ring having 3-10 ring atoms; or
- R and R' or two occurrences of either R or R' are taken together with the atoms to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or

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two occurrences of either R' or R on the same nitrogen are taken together with the nitrogen atom to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

 R^2 is hydrogen, CN, -SR, -OR, -CO₂R, -OC(O)R, -C(O)R, -C(O)N(R)₂, -N(R)₂, or -N(R)C(O)R, or an optionally substituted C₁₋₆ aliphatic group;

T is CR^3 ;

each of A¹, A², and A³ is, independently, CR⁴;

 R^3 is selected from hydrogen, halogen, NO₂, CN, -SR, -OR, -N(R)₂, or an optionally substituted C_{1-6} aliphatic group; and

R⁴ is selected from halogen, NO₂, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; or two R⁴ groups on adjacent atoms are taken together to form an optionally substituted 5-7 membered partially unsaturated or fully unsaturated ring having 0-3 heteroatoms independently selected from oxygen, sulfur, or nitrogen, wherein;

each ring formed by two R⁴ groups on adjacent atoms taken together is optionally substituted with up to 4 occurrences of Z-R^X.

48. (Canceled)

49. (Currently amended) The composition of claim 47, additionally comprising a therapeutic agent selected from a chemotherapeutic or anti-proliferative agent mechlorethamine, chlorambucil, cyclophosphamide, melphalan, ifosfamide, methotrexate, 6-mercaptopurine, 5-fluorouracil, cytarabile, gemcitabine, vinblastine, vincristine, vinorelbine, paclitaxel, etoposide, irinotecan, topotecan, doxorubicin, bleomycin, mitomycin, carmustine, lomustine, cisplatin, carboplatin, asparaginase, and tamoxifen, leuprolide, flutamide, megestrol, imatinib (GleevecTM), adriamycin,

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dexamethasone, or cyclophosphamide, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders.

50. (Currently amended) A method of inhibiting CDK-2, c-MET, FLT-3, JAK-3, GSK-3, IRAK-4, SYK, p70S6K, TAK-1, or ZAP-70 kinase activity in a biological sample, wherein said biological sample is selected from a cell culture, biopsied material obtained from a mammal, saliva, urine, feces, semen, or tears, or an extract thereof; which method comprises contacting said biological sample with a composition according to claim 47 or a compound of formula I:

$$A^{1} \xrightarrow{R^{2}} O \xrightarrow{R^{1}}$$

or a pharmaceutically acceptable salt thereof, wherein:

 R^{1} is $-(L)_{m}R$, $-(L)_{m}Ar^{1}$, or $-(L)_{m}Cy^{1}$;

L is -S-, -O-, -N(R)-, or a C_{1-6} alkylidene chain wherein up to two non-adjacent methylene units of L are optionally and independently replaced by -S-, -O-, -N(R)-, -N(R)C(O)-,

 $-N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO_2-, -C(O)-, -CO_2-, -C(O)-, -C(O$

 $-C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO_2-, -SO_2N(R)-, -N(R)SO_2-, \\$

 $-N(R)SO_2N(R)$ -, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or $-C(O)CH_2C(O)$ -; m is 0 or 1;

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Ar¹ is an optionally substituted 5-7 membered monocyclic ring or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Cy¹ is an optionally substituted 3-7 membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein;

 $-N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO_2-, -C(O)-,$

 $-CO_2-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO_2-, -SO_2N(R)-, -N(R)SO_2-, -SO_2N(R)-, -N(R)SO_2-, -N(R)SO_2-,$

 $-N(R)SO_2N(R)-,\ -C(R)=NN(R)-,\ -C(R)=N-O(R)-,\ -C(O)C(O)-,\ or\ -C(O)CH_2C(O)-;$

each occurrence of RX is independently selected from -R', halogen, NO2, CN, -OR', -SR',

 $-N(R')_2$, -N(R')C(O)R', -N(R')C(S)R', $-N(R')C(O)N(R')_2$, $-N(R')C(S)N(R')_2$,

 $-N(R')CO_2R'$, -C(O)R', -C(S)R', $-CO_2R'$, -OC(O)R', $-C(O)N(R')_2$, $-C(S)N(R')_2$,

 $-OC(O)N(R')_2$, -S(O)R', $-SO_2R'$, $-S(O)_3R'$; $-SO_2N(R')_2$, $-N(R')SO_2R'$,

 $-N(R')SO_2N(R')_2$, -C(O)C(O)R', $-C(O)CH_2C(O)R'$, -NR'NR'C(O)R',

-NR'NR'C(O)N(R')₂, -NR'NR'CO₂R', -C(O)N(OR') R', -C(NOR') R', -S(O)₃R,

-N(OR')R', $-C(=NH)-N(R')_2$; or $-(CH_2)_{0-2}NHC(O)R'$; wherein

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group,

each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, an optionally substituted C_{6-10} aryl ring, an optionally substituted heteroaryl ring having 5-10 ring atoms, or an optionally substituted heterocyclyl ring having 3-10 ring atoms; or

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R and R' or two occurrences of either R or R' are taken together with the atoms to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or

two occurrences of either R' or R on the same nitrogen are taken together with the nitrogen atom to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

 R^2 is hydrogen, CN, -SR, -OR, -CO₂R, -OC(O)R, -C(O)R, -C(O)N(R)₂, -N(R)₂, -N(R)C(O)R, or an optionally substituted C₁₋₆ aliphatic group;

T is CR³;

each of A¹, A², and A³ is, independently, CR⁴;

 R^3 is selected from hydrogen, halogen, NO₂, CN, -SR, -OR, -N(R)₂, or an optionally substituted C_{1-6} aliphatic group; and

R⁴ is selected from halogen, NO₂, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; or two R⁴ groups on adjacent atoms are taken together to form an optionally substituted 5-7 membered partially unsaturated or fully unsaturated ring having 0-3 heteroatoms independently selected from oxygen, sulfur, or nitrogen, wherein;

each ring formed by two R⁴ groups on adjacent atoms taken together is optionally substituted with up to 4 occurrences of Z-R^X.

51. (Canceled)

52. (Currently amended) A method of treating or lessening the severity of a disease or condition in a patient selected from gastric cancer, pancreatic cancer, ovarian cancer,

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<u>breast cancer</u>, or <u>prostate cancer</u> <u>cancer or a proliferative disorder</u> comprising the step of administering to said patient a composition of claim 47.

53. (Currently amended) The method according to claim 52, comprising the additional step of administering to said patient an additional therapeutic agent selected from mechlorethamine, chlorambucil, cyclophosphamide, melphalan, ifosfamide, methotrexate, 6-mercaptopurine, 5-fluorouracil, cytarabile, gemcitabine, vinblastine, vincristine, vinorelbine, paclitaxel, etoposide, irinotecan, topotecan, doxorubicin, bleomycin, mitomycin, carmustine, lomustine, cisplatin, carboplatin, asparaginase, and tamoxifen, leuprolide, flutamide, megestrol, imatinib (GleevecTM), adriamycin, dexamethasone, or cyclophosphamide a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders, wherein:

said additional therapeutic agent is appropriate for the disease being treated; and said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.

54-58. (Canceled)

59. (Currently amended) The composition according to claim 47, wherein R¹ is -(L)_mAr¹ and Ar¹ is selected from one of the following groups:

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$$Z_{Z_{2}}$$
 $Z_{Z_{2}}$
 $Z_{Z_{2}}$

wherein x is 0-5.

60. (Currently amended) The composition according to claim 59, wherein Ar¹ is selected from one of the following groups:

wherein x is 0-5.

61. (Previously presented) The composition according to claim 59, wherein R^1 is $-(L)_m$ -Ar 1 , m is 1 and compounds have the formula IA-1:

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62. (Currently amended) The composition according to claim 59, wherein Ar¹ is phenyl with 0-5 occurrences of ZR^X and compounds have the formula **IA-1-5**:

$$A^{1} \xrightarrow{X} O (L)_{m} \xrightarrow{(ZR^{X})_{x}} (ZR^{X})_{x}$$

IA-1-5,

wherein x is 0-5.

63. (Previously presented) The composition according to claim 47, wherein R¹ is -(L)_m-Cy¹ and compounds have the formula IA-2:

64. (Currently amended) The composition according to claim 63, wherein Cy¹ is selected from one of the following groups:

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wherein x is 0-5.

- 65. (Previously presented) The composition according to claim 59, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).
- 66. (Previously presented) The composition according to claim 65, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, CO, CONR, SO₂NR, NRSO₂.
- 67. (Previously presented) The composition according to claim 47, wherein R¹ is -(L)_mR, L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, and R is an optionally substituted C₁₋₆ aliphatic group.
- 68. (Currently amended) The composition according to claim 47, wherein R^2 is hydrogen, -CN, -OR, -CO₂R, -OC(O)R, -C(O)R, -C(O)N(R)₂, -N(R)₂, or -N(R)C(O)R, or an optionally substituted C_{1-6} aliphatic group.

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69-70. (Canceled)

71. (Previously presented) The composition according to claim 47, wherein R² is hydrogen and compounds have the formula **IB**:

$$A^{1} \xrightarrow{R^{2}} A^{3} \xrightarrow{O} R^{1}$$

$$IB.$$

- 72. (Previously presented) The composition according to claim 47, wherein T is CR^3 and R^3 is hydrogen, halogen, CN, or an optionally substituted C_{1-6} aliphatic group.
- 73. (Previously presented) The composition according to claim 72, wherein R³ is hydrogen, halogen, CF₃, methyl, ethyl, n-propyl, isopropyl, or cyclopropyl.
- 74. (Previously presented) The composition according to claim 47, wherein T is CR³, R³ is hydrogen and compounds have the formula **IC**:

$$A^{1}$$

$$A^{2}$$

$$A^{3}$$

$$O$$

$$R^{1}$$

IC.

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75. (Previously presented) The composition according to claim 47, wherein A^1 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.

- 76. (Previously presented) The composition according to claim 75, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).
- 77. (Previously presented) The composition according to claim 75, wherein A¹ is CR⁴ and R⁴ is halogen, CN, or R.
- 78. (Previously presented) The composition according to claim 75, wherein A^1 is CR^4 , R^4 is $-(L)_mR$, and compounds have the formula **ID-1**:

79. (Previously presented) The composition according to claim 75, wherein A^{1} is CR^{4} , R^{4} is $-(L)_{m}Ar^{1}$, and compounds have the formula **ID-2**:

$$Ar_{\parallel}^{1}$$
 $N(OH)$ R^{2} A^{2} A^{3} O R^{1} R^{2} R^{2} R^{2}

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80. (Previously presented) The composition according to claim 75, wherein A^1 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula **ID-3**:

$$Cy^1$$
 $N(OH)$ R^2 A^2 O R^1 $D-3$.

- 81. (Previously presented) The composition according to claim 47, wherein A^2 is CR^4 and R^4 is halogen, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹.
- 82. (Previously presented) The composition according to claim 81, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).
- 83. (Previously presented) The composition according to claim 81, wherein A² is CR⁴ and R⁴ is halogen or R.
- 84. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 and R^4 is $-(L)_mR$, wherein L is -O- or -N(R)-.
- 85. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mCy^1$, m is 0 and Cy^1 is 2-2, 2-5, 2-6, 2-7, 2-8, or 2-12.

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- 86. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mAr^1$, m is 0 and Ar^1 is 1-5, 1-6, 1-11, 1-12, 1-13, 1-19, 1-24, or 1-25.
- 87. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mR$, and compounds have the formula **IE-1**:

$$\begin{array}{c|c}
 & N(OH) \\
 & R^2 \\
 & R^1
\end{array}$$

IE-1.

88. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mAr^1$, and compounds have the formula **IE-2**:

IE-2.

89. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula **IE-3**:

E-3

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- 90. (Previously presented) The composition according to claim 47, wherein A^3 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.
- 91. (Previously presented) The composition according to claim 90, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).
- 92. (Previously presented) The composition according to claim 90, wherein A³ is CR⁴ and R⁴ is halogen or R.
- 93. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 and R^4 is $-(L)_mR$, wherein L is -O- or -N(R)-.
- 94. (Previously presented) The composition according to claim 90, A^3 is CR^4 , R^4 is $-(L)_mCy^1$, m is 0 and Cy^1 is 2-2, 2-5, 2-6, 2-7, 2-8, or 2-12.
- 95. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mAr^1$, m is 0 and Ar^1 is 1-5, 1-6, 1-11, 1-12, 1-13, 1-19, 1-24, or 1-25.

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96. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mR$, and compounds have the formula **IF-1**:

97. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mAr^1$, and compounds have the formula **IF-2**:

$$Ar^{1-(L)_m} I$$

IF-2.

98. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula **IF-3**:

$$R^{1}$$
 R^{2}
 R^{1}
 R^{2}
 R^{1}
 R^{2}
 R^{1}
 R^{1}
 R^{2}
 R^{1}
 R^{2}

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99. (Previously presented) The composition according to claim 47, wherein T is CR³, A¹, A² and A³ are each CR⁴ and compounds have the formula **IG-1**:

$$R^4$$
 R^4
 R^4
 R^4
 R^4
 R^4
 R^4
 R^4
 R^4

IG-1.

100. (Previously presented) The composition according to claim 47, wherein each ZR^X is independently halogen, NO₂, CN, or an optionally substituted group selected from C₁₋₄ alkyl, aryl, aralkyl, -N(R')₂, -CH₂N(R')₂, -OR', -CH₂OR', -SR', -CH₂SR', -COOR', or -S(O)₂N(R')₂.

101. (Currently amended) The composition according to claim 47, selected from one of the following compounds:

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